Health Advisory:

Q Fever Cases in Missouri

March 27, 2014

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Health Advisory
March 27, 2014

FROM: GAIL VASTERLING
DIRECTOR

SUBJECT: Q Fever Cases in Missouri

Q fever is a zoonotic disease caused by the bacteria *Coxiella burnetii*. *C. burnetii* is distributed worldwide and causes sporadic infections and outbreaks in animal species and humans. In 2013, 22 human Q fever cases were reported to the Missouri Department of Health and Senior Services (DHSS). The purpose of this DHSS Health Advisory is to increase awareness among health care providers of Q fever, and to provide guidance on the epidemiology, diagnosis, and treatment of Q fever, including the identification of persons who are at higher risk of Q fever infection and its complications.

Background

C. burnetii are spore-forming bacteria that can survive for long periods of time in the environment. The primary sources of Q fever are infected cattle, sheep, and goats, which shed the organism in feces, milk, nasal discharge, placental tissue, and amniotic fluid. *C. burnetii* is known to be present in roughly 20-30% of goat herds, and is also endemic in cattle and sheep. Infection of humans usually occurs by inhalation of *C. burnetii* from air that contains airborne barnyard dust contaminated by infected animals. Inhalation of just a single organism is sufficient to cause infection. Cases of Q fever have been documented among people living downwind from infected livestock without having direct exposure to infected animals. Other, less common routes of transmission include: the consumption of raw dairy products, human-to-human transmission (baby infected during delivery by infected mother, exposure during autopsy), or a blood transfusion from an infected donor. Ticks can harbor *C. burnetii*, but infections acquired through a tick bite are rare. Because of the high infectivity of this organism, *C. burnetii* is designated a Category B bioterrorism agent.

Human cases are rare, with typically fewer than 200 Q fever cases reported annually in the United States, and 0-5 cases per year reported in Missouri between 2008 and 2012. However, because Q fever may resemble other diseases, be mild, or even cause no symptoms (asymptomatic seroconversion occurs in 50-60% of infected persons), cases of human Q fever are likely under-recognized. Q fever outbreaks associated with animal farms have been reported in the United States.

Q fever can cause acute and chronic illness in humans. Illness onset typically occurs 2-3 weeks after exposure to the organism. Symptoms may include: high fever (104°-105° F), chills and/or sweats, severe headache, malaise, myalgia, non-productive cough, chest pain, and possibly gastrointestinal symptoms such as nausea, vomiting, diarrhea, or abdominal pain. Most acute Q fever cases will recover completely, but some persons experience serious illness and severe complications, including: pneumonia, granulomatous hepatitis, myocarditis, and central nervous system complications. Pregnant women who are infected may be at risk for pre-term delivery or miscarriage. The estimated case fatality rate is < 2% of hospitalized patients. Early treatment with an appropriate antibiotic may shorten the duration of illness and lessen the risk of complications.

Chronic Q fever is a severe disease occurring in < 5% of acutely infected patients. It may occur as early as six weeks after an acute infection, or may manifest years later. Chronic Q fever is a risk for anyone with a history of acute Q fever illness, particularly those persons

with **valvular disease**, **blood vessel abnormalities**, **immunosuppressed** persons (such as may occur through cancer treatments, advanced HIV infection, prior organ transplants, or some medications), and women who were **pregnant** when they became infected. Endocarditis is the major form of chronic disease, comprising 60-70% of all reported cases, and with an estimated case fatality rate in untreated patients of 25-60%. Other forms of chronic Q fever include aortic aneurysms and infections of the bone, liver, or reproductive organs, such as the testes in males.

Post-Q fever fatigue syndrome has been reported to occur in 10-25% of some acute patients. This syndrome is characterized by constant or recurring fatigue, night sweats, severe headaches, photophobia, pain in muscles and joints, mood changes, and difficulty sleeping.

Diagnosis

Healthcare providers must use their judgment to treat patients based on clinical suspicion alone. While Q fever should be considered in patients who have close contact with domestic ruminants and cats, such an exposure may not always be reported. Information such as recent travel to rural or agricultural communities where infected livestock may be present, or employment in high risk occupations such as veterinarians or farmers, can be helpful in making the diagnosis. Clues such as a prolonged fever with low platelet count, normal leukocyte count, and elevated liver enzymes are suggestive of acute Q fever infection. Diagnosis can later be confirmed using specialized confirmatory laboratory tests. *Treatment should never be delayed pending the receipt of laboratory test results, or be withheld on the basis of an initial negative laboratory result.*

Laboratory Diagnosis

Clinical diagnoses of Q fever are confirmed by **serological** testing or **polymerase chain reaction** (PCR) where available.

Antibody titers to *C. burnetii* are usually detectable by 7-10 days after illness onset, and a negative test during the first week of illness does not rule out Q fever as a cause of illness. There are two distinct antigenic phases (Phase I and Phase II) to which humans develop antibody responses. In acute infection, an antibody response to *C. burnetii* Phase II antigen is predominant and is higher than Phase I antibody response; the reverse is true in chronic infection which is associated with a rising Phase I IgG titer that is often much higher than Phase II IgG. The gold standard serologic test for diagnosis of acute Q fever is the indirect immunofluorescence assay (IFA) using *C. burnetii* antigen. The first sample should be taken as early in the disease as possible, preferably in the first week of symptoms, and the second sample should be taken 2 to 4 weeks later. IgM antibodies usually rise at the same time as IgG near the end of the first week of illness and remain elevated for months or longer. Also, IgM antibodies are more likely to result in a false positive result. **Physicians should request both Phase I and Phase II IgG and IgM serologic titers** for diagnostic confirmation of acute and chronic Q fever. Approximately 3% of currently healthy people in the U.S. general population and up to 20% of people in high-risk professions (veterinarians, ranchers, etc.) have elevated antibody titers due to past exposure to *C. burnetii*. Therefore, **if only one sample is tested it can be difficult to interpret the findings. Paired samples** taken 2-4 weeks apart demonstrating a significant (four-fold) rise in antibody titer provide the **best evidence** for a correct diagnosis of acute Q fever. Diagnosis of chronic Q fever is confirmed by elevated Phase I IgG antibody (current U.S. case definitions >1:800 and higher than Phase II IgG) **and** an identifiable persistent focus of infection (e.g., endocarditis). Elevated Phase I titers alone do not confirm a chronic Q fever diagnosis.

During the acute phase of illness, a sample of whole blood can be tested by PCR assay to determine if a patient has Q fever. PCR is most sensitive in the first week of illness, and decreases in sensitivity following the administration of appropriate antibiotics. Although a positive PCR result is helpful, a negative result does not rule out the diagnosis, and treatment should not be withheld due to a negative result.

Culture isolation of *C. burnetii* is only available at specialized laboratories; **routine hospital blood cultures cannot detect the organism.**

The Missouri State Public Health Laboratory (MSPHL) can perform PCR assays on whole blood samples taken during the first week of illness and prior to initiation of antibiotic therapy, with prior arrangements. Testing requested on additional samples other than blood will be conducted at the Centers for Disease Control and Prevention (CDC) in Atlanta, GA. Please contact the Virology unit at MSPHL by calling 573/751-3334 for assistance.

Treatment

Doxycycline is the first line treatment for all adults and for children with severe illness. Treatment should be initiated immediately whenever Q fever is suspected. Use of antibiotics other than doxycycline or other tetracyclines is associated with a higher risk of severe illness. Doxycycline is most effective at preventing severe complications if it is started early in the course of disease. Failure to respond to doxycycline suggests that the patient's condition might not be due to Q fever.

Recommended Dosage for Acute Q fever

Doxycycline is the first line treatment for children with severe illness of all ages and adults:

- Adults: 100 mg every 12 hours
- Children under 45 kg (100 lbs): 2.2 mg/kg body weight given twice a day

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Standard duration of treatment is 2-3 weeks.

Recommended Dosage for Chronic Q fever

- Adults: Doxycycline 100 mg every 12 hours and hydroxychloroquine 200 mg every 8 hours.

Standard duration of treatment is 18 months.

The use of doxycycline is recommended to treat Q fever in children of all ages who are hospitalized or are severely ill. Children with mild illness who are less than 8 years of age may be treated with co-trimoxazole, but therapy should be switched to doxycycline if their course of illness worsens.

Treatment of pregnant women diagnosed with acute Q fever with once daily co-trimoxazole throughout pregnancy has been shown to significantly decrease the risk of adverse consequences for the fetus.

Patients at highest risk for progression to chronic Q fever should be serologically and clinically monitored at intervals of 3, 6, 12, 18, and 24 months after diagnosis of acute Q fever. Patients without obvious risk factors for chronic Q fever should receive a clinical and serologic follow-up approximately 6 months after diagnosis of acute illness to identify potential progression to chronic disease.

The prophylactic antimicrobial treatment for prevention of Q fever after a known exposure and prior to symptom onset is not indicated. Attempts at prophylaxis will likely extend the incubation period but will not prevent infection from occurring.

Please report any suspected Q fever cases within 1 day to your local public health agency (LPHA), or to DHSS at 573/751-6113.

References:

1. Centers for Disease Control and Prevention (CDC). Notes from the Field: Q Fever Outbreak Associated with Goat Farms — Washington and Montana, 2011. *Morbidity and Mortality Weekly Report* 2011; 60(40); 1393. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6040a5.htm.

2. Centers for Disease Control and Prevention (CDC). Diagnosis and Management of Q Fever — United States, 2013: Recommendations from CDC and the Q Fever Working Group. *Morbidity and Mortality Weekly Report* 2013; **62(RR03);1-23.** Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6203a1.htm.

3. Centers for Disease Control and Prevention (CDC). Q fever Homepage. Go to http://www.cdc.gov/qfever/.

Health Advisory:

Confirmed Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Case in Indiana, 2014

May 6, 2014

This document will be updated as new information becomes available. The current version can always be viewed at http://www.health.mo.gov

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Health Advisory
May 6, 2014

FROM: **GAIL VASTERLING**
DIRECTOR

SUBJECT: **Confirmed Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Case in Indiana, 2014**

On May 3, 2014, the Centers for Disease Control and Prevention (CDC) issued a Health Advisory describing the first case of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection in the United States, which was recently identified in Indiana in a traveler from Saudi Arabia. The CDC Health Advisory encourages medical providers to increase their index of suspicion for the possibility of MERS-CoV infection in travelers from the Arabian Peninsula and neighboring countries. It also provides guidance on the identification and evaluation of possible cases, and on appropriate infection control practices.

No suspected cases of MERS-CoV infection have been reported in Missouri.

The CDC Health Advisory is reproduced below with some added information from the Missouri Department of Health and Senior Services (DHSS) for Missouri medical providers and laboratories.

Confirmed Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Case in Indiana, 2014

Distributed via the CDC Health Alert Network
May 3, 2014

Summary

The first case of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection in the United States, identified in a traveler, was reported to CDC by the Indiana State Department of Health (ISDH) on May 1, 2014, and confirmed by CDC on May 2. The patient is in a hospital in Indiana after having flown from Saudi Arabia to Chicago via London. The purpose of this HAN is to alert clinicians, health officials, and others to increase their index of suspicion to consider MERS-CoV infection in travelers from the Arabian Peninsula and neighboring countries. Please disseminate this information to infectious disease specialists, intensive care physicians, primary care physicians, and infection preventionists, as well as to emergency departments and microbiology laboratories.

Background

The first known cases of MERS-CoV occurred in Jordan in April 2012. The virus is associated with respiratory illness and high death rates, although mild and asymptomatic infections have been reported too. All reported cases to date have been linked to six countries in the Arabian Peninsula: Saudi Arabia, Qatar, Jordan, the United Arab Emirates (UAE), Oman, and Kuwait. Cases in the United

Kingdom, France, Italy, Greece, Tunisia, Egypt, and Malaysia have also been reported in persons who traveled from the Arabian Peninsula. In addition, there have been a small number of cases in persons who were in close contact with those infected travelers. Since mid-March 2014, there has been an increase in cases reported from Saudi Arabia and UAE. Public health investigations are ongoing to determine the reason for the increased cases. There is no vaccine yet available and no specific treatment recommended for the virus. In some cases, the virus has spread from infected people to others through close contact. However, there is currently no evidence of sustained spread of MERS-CoV in community settings. Additional information is available at (http://www.cdc.gov/coronavirus/mers/index.html).

Recommendations

Healthcare providers should be alert for and evaluate patients for MERS-CoV infection who 1) develop severe acute lower respiratory illness within 14 days after traveling from countries in or near the Arabian Peninsula, excluding those who only transited at airports in the region; or 2) are close contacts of a symptomatic recent traveler from this area who has fever and acute respiratory illness; or 3) are close contacts of a confirmed case. For these patients, testing for MERS-CoV and other respiratory pathogens can be done simultaneously. Positive results for another respiratory pathogen (e.g., H1N1 Influenza) should not necessarily preclude testing for MERS-CoV because co-infection can occur.

Clusters of patients with severe acute respiratory illness (e.g., fever and pneumonia requiring hospitalization) without recognized links to cases of MERS-CoV or to travelers from countries in or near the Arabian Peninsula should be evaluated for common respiratory pathogens. If the illnesses remain unexplained, providers should consider testing for MERS-CoV, in consultation with state and local health departments. Healthcare professionals should immediately report to their state or local health department any person being evaluated for MERS-CoV infection as a patient under investigation (PUI). Additional information, including criteria for PUI are at http://www.cdc.gov/coronavirus/mers/interim-guidance.html. Healthcare providers should contact their state or local health department if they have any questions.

Persons at highest risk of developing infection are those with close contact to a case, defined as any person who provided care for a patient, including a healthcare provider or family member not adhering to recommended infection control precautions (i.e., not wearing recommended personal protective equipment), or had similarly close physical contact; or any person who stayed at the same place (e.g. lived with, visited) as the patient while the patient was ill.

Healthcare professionals should carefully monitor for the appearance of fever (T> 100F) or respiratory symptoms in any person who has had close contact with a confirmed case, probable case, or a PUI while the person was ill. If fever or respiratory symptoms develop within the first 14 days following the contact, the individual should be evaluated for MERS-CoV infection. Ill people who are being evaluated for MERS-CoV infection and do not require hospitalization for medical reasons may be cared for and isolated in their home. (Isolation is defined as the separation or restriction of activities of an ill person with a contagious disease from those who are well.). Providers should contact their state or local health department to determine whether home isolation, home quarantine or additional guidance is indicated since recommendations may be modified as more data becomes available. Additional information on home care and isolation guidance is available at http://www.cdc.gov/coronavirus/mers/hcp/home-care.html. Healthcare providers should adhere to recommended infection-control measures, including standard, contact, and airborne precautions, while managing symptomatic contacts and patients who are persons under investigation or who have

probable or confirmed MERS-CoV infections. For CDC guidance on MERS-CoV infection control in healthcare settings, see Interim Infection Prevention and Control Recommendations for Hospitalized Patients with MERS-CoV at http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html.

Providers should notify their state or local health departments if they suspect MERS-CoV infection in a person. State or local health departments should notify CDC if MERS-CoV infection in a person is suspected. Additional information is available at http://www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html.

> If a Missouri medical provider has a patient that appears to meet the above-mentioned CDC criteria for who should be evaluated for MERS-CoV, that provider should immediately contact DHSS at 800/392-0272 (24/7). The provider will be directed to the department's Bureau of Communicable Disease Control and Prevention (BCDCP) to discuss sending specimens for testing at the Missouri State Public Health Laboratory (MSPHL). **Note that before any specimen is sent for testing, BCDCP staff must first be consulted at 800/392-0272.** After consultation with BCDCP and determination has been made that the patient meets the criteria for testing, the medical provider should then contact the MSPHL at 573/751-3334 or 800/392-0272 for guidance on specimen collection and shipping prior to collecting the specimens. This will help ensure that proper specimens are obtained in the right quantity, and that they are packed and transported properly.

For suspected MERS-CoV cases, healthcare providers should collect the following specimens for submission to CDC or the appropriate state public health laboratory: nasopharyngeal swab, oropharyngeal swab (which can be placed in the same tube of viral transport medium), sputum, serum, and stool/rectal swab. All of the swabs mentioned above must be Dacron swabs. Recommended infection control precautions should be utilized when collecting specimens. Specimens can be sent using category B shipping containers.

Additional or modified recommendations may be forthcoming as the investigation proceeds.

For More Information

For more information, for consultation, or to report possible cases, please contact the CDC Emergency Operations Center at 770/488-7100.

For Missouri providers, questions can be directed to DHSS' Bureau of Communicable Disease Control and Prevention at 573/751- 6113, or 800/392-0272 (24/7).

Health Advisory:

Record Number of Reported Measles Cases in the U.S. in 2014

June 6, 2014

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Health Advisory
June 6, 2014

FROM: GAIL VASTERLING
DIRECTOR

SUBJECT: Record Number of Reported Measles Cases in the U.S. in 2014

On May 29, 2014, the Centers for Disease Control and Prevention (CDC) issued a press release entitled "Measles Cases in the United States Reach 20-Year High." A brief summary of the press release along with other pertinent information is provided below.

Summary and Background

Three hundred thirty-four cases of measles were reported to the Centers for Disease Control and Prevention (CDC) in the United States between Jan. 1 and May 30, 2014. This is the largest number of measles cases in the United States reported in the first five months of a year since 1994. Missouri is one of many states reporting measles cases this year. Nearly all of the measles cases this year have been associated with international travel by unvaccinated persons or persons whose vaccination status was unknown.

The large number of measles cases this year stresses the importance of vaccination. Healthcare providers should use every patient encounter to ensure that all patients are up to date on vaccinations; especially before international travel. Travelers with measles continue to bring the disease into the U.S., which can then spread to communities or groups of people who are unvaccinated.

Measles was declared eliminated in the U.S. in 2000 due to high 2-dose measles vaccine coverage, but it is still endemic, or large outbreaks are occurring, in countries in Europe (including France, the United Kingdom, Spain, and Switzerland), Africa, Asia (including India), and the Philippines. The increase in measles cases and outbreaks in the U.S. this year underscores the ongoing risk of importations, the need for high measles vaccine coverage, and the importance of prompt and appropriate public health response to measles cases and outbreaks.

Measles is a highly contagious, acute viral illness that is transmitted by contact with an infected person through coughing and sneezing. Patients are considered to be contagious from 4 days before until 4 days after the rash appears. After an infected person leaves a location, the virus remains contagious for up to 2 hours on surfaces and in the air. Measles can cause severe health complications, including pneumonia, encephalitis, and death.

Recommendations for Health Care Providers.

Exposure to measles is not a contraindication to immunization. Available data suggest that the measles vaccine, if given within 72 hours of measles exposure, will provide protection in some cases. If the exposure does not result in infection, the vaccine should induce protection against subsequent measles exposures. (*MMWR*, June 14, 2013 / 62(RR04);1-34)

For those who travel abroad, CDC recommends that all U.S. residents older than 6 months be protected against measles and receive the MMR vaccine, if needed, prior to departure.

- Infants 6 through 11 months old should receive 1 dose of the MMR vaccine before departure.*

- Children 12 months of age or older should have documentation of 2 doses of the MMR vaccine (separated by at least 28 days).
- Children 1 through 12 years of age may receive the MMRV vaccine for protection against measles, mumps, rubella, and varicella; however, MMRV vaccine is not recommended for the first dose in the MMR series of vaccinations for children ages 12 months through 47 months.** CDC recommends that the MMR vaccine and the varicella vaccine be administered separately for the first dose in this age group. Providers who are considering administering MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers.
- Teenagers and adults without evidence of measles immunity† should have documentation of 2 appropriately spaced doses of the MMR vaccine.

Health-care providers should maintain a high suspicion for measles among febrile patients with a rash. Patients with clinical symptoms compatible with measles (febrile rash plus cough, coryza, and/or conjunctivitis, should be asked about recent travel abroad and contact with returning travelers, or contact with someone with a febrile rash illness. Their vaccination status should also be verified. Immunocompromised patients may not exhibit rash or may exhibit an atypical rash. The incubation period for measles from exposure to fever is usually about 10 days (range, 7 to 14 days) and from exposure to rash onset is usually 14 days (range, 7 to 21 days).

Persons who have been exposed to measles should contact their healthcare provider if they develop cold-like symptoms with a fever and/or rash. They should **NOT** go to any healthcare facility without calling first. The suspect case should be kept separate from others to prevent further spread.

Isolate suspect measles case-patients and immediately report suspected cases to the local public health agency, or to the Missouri Department of Health and Senior Services (DHSS) at 573/751-6113 or 800/392-0272 (24/7). To ensure a prompt public health response, do not wait for laboratory confirmation.

Laboratory specimens may be referred to the Missouri State Public Health Laboratory after consultation with the local public health agency or DHSS representative. Obtain a single blood/serum specimen for measles IgM serology testing. A specimen for RT-PCR (throat swab, NP swab, urine) **must** be collected for simultaneous submission with the serum specimen. For more information, please call 573/751-3334.

The sensitivity of measles IgM assays varies and may be diminished during the first 72 hours after rash onset. If the result is negative for measles IgM and the patient has a generalized rash lasting more than 72 hours, a second serum specimen should be obtained and the measles IgM test should be repeated. (AAP. *Red Book*, 2012; p. 491)

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* Infants who receive a dose of MMR vaccine before their first birthday should receive 2 more doses of MMR vaccine, the first of which should be administered when the child is 12 through 15 months of age and the second at least 28 days later.

**In MMRV vaccine pre-licensure studies conducted among children 12-23 months of age, fever (reported as abnormal or elevated 102°F or higher oral equivalent) was observed 5-12 days after vaccination in 21.5% of MMRV vaccine recipients compared with 14.9% of recipients who received MMR vaccine and varicella vaccine separately.

† One of the following is considered evidence of measles immunity for international travelers: (1) Documentation of age-appropriate vaccination with a live measles virus-containing vaccine: for infants aged 6–11 months: 1 dose, for persons aged ≥12 months: 2 doses; or (2) Laboratory evidence of immunity; or (3) Laboratory confirmation of disease; or (4) Born before 1957. For further guidance, please refer to http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm?s_cid=rr6204a1_w.

Questions should be directed to DHSS' Bureau of Immunization Assessment and Assurance at 573/751-6124.

For more information:

Measles Cases and Outbreaks:
http://www.cdc.gov/measles/cases-outbreaks.html

For Healthcare Professionals:
http://www.cdc.gov/measles/hcp/index.html

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm?s_cid=rr6204a1_w

For Travelers:
http://www.cdc.gov/measles/travelers.html

Laboratory Information:
http://health.mo.gov/lab/measlesrubella.php (IgM serology)

http://health.mo.gov/lab/measles.php (measles isolation/RT-PCR)

Health Advisory:

Rabies Threat in Missouri

June 24, 2014

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Health Advisory
June 24, 2014

FROM: **GAIL VASTERLING**
DIRECTOR

SUBJECT: **Rabies Threat in Missouri**

Current Situation

Animal rabies occurs year-round in Missouri, but has its highest incidence during late-spring, throughout the summer, and into early-fall since wild animals are most active during these seasons. Increased human outdoor activity coincides with that of wild animals during these warmer months, resulting in significant opportunities for people to be exposed to the rabies virus. People can also be exposed to rabies by encountering stray dogs and cats in the community, by wild animals (such as bats) entering homes, and by unvaccinated dogs and cats that have been allowed to roam freely bringing it into the household. Persons bitten by any mammal or otherwise possibly exposed to rabies virus should be evaluated by a medical provider to determine if rabies post-exposure prophylaxis (RPEP) is indicated. Patients who have experienced a bite from an animal should also receive additional standard medical care as needed, such as thorough wound cleansing, antibiotic coverage, and assessment of tetanus vaccination status. The purpose of this health advisory is to: 1) emphasize the importance of conducting a rabies risk assessment following the potential exposure of a patient to rabies virus; 2) review risk factors of rabies transmission as they relate to decisions regarding the need for RPEP; 3) provide guidance and support in the medical follow-up of suspect cases of human rabies; and 4) to list resources available to health care providers and others involved with the prevention of human rabies.

Incidence of Rabies in Missouri

Rabies is endemic in wildlife in Missouri, the main reservoirs being bats and skunks. Approximately 50 rabid wild and domestic animals are detected annually in Missouri. However, this number underestimates the true incidence since testing is only conducted in situations where a public health or medical decision needs to be made. Over the past ten years (2004-2013), bats have accounted for about 71 percent of the rabid animals detected while skunks accounted for approximately 26 percent. Other rabid animals detected during this ten-year period included six horses, five dogs, four cats, one cow, and one goat. Rabid bats may be found anywhere in Missouri. Rabid skunks may also be found anywhere in the state, but most detections occur in the southern half of Missouri. Additional information pertaining to rabies in Missouri may be found at www.health.mo.gov/rabies. The last human rabies death in Missouri, which occurred in 2008, involved a Texas County resident who was bitten by a bat and who failed to seek medical treatment following the bite. A complete description of this case can be found in the Centers for Disease Control and Prevention's *Morbidity and Mortality Weekly Report (MMWR)*, November 6, 2009/58(43);1207-1209 (www.cdc.gov/mmwr/preview/mmwrhtml/mm5843a3.htm).

Rabies Risk Assessment

1. Rabies risk assessments should be conducted in accordance with *Human Rabies Prevention – United States, 2008, Recommendations of the Advisory Committee on*

Immunization Practices (www.cdc.gov/mmwr/PDF/rr/rr5703.pdf) and *Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies, Recommendations of the Advisory Committee on Immunization Practices* (www.cdc.gov/mmwr/pdf/rr/rr5902.pdf).

2. Persons with possible rabies exposure should be evaluated as soon as possible by a health care provider. Providers are encouraged to consult with local and state health officials regarding the need for RPEP. RPEP is normally considered to be an urgent medical issue and not usually an emergency. Therefore, it can sometimes be delayed until rabies testing or clinical observation of the biting animal during a quarantine period is completed. Whether the animal is tested or placed under quarantine depends upon the species of biting animal and other risk factors as described below. This approach helps ensure that only persons with actual or highly suspected rabies exposure are given RPEP, thus saving money and conserving limited resources.

3. Variables to consider when conducting a rabies risk assessment include the type of exposure (bite or nonbite), species of biting animal, severity and location of the wound, and circumstances surrounding the incident (provoked or unprovoked).

   a) Type of Exposure (Bite or Nonbite): Rabies is carried and transmitted only by mammals. Bite wounds are the most common means of rabies transmission and require RPEP more often than nonbite exposures. Even a minor wound is sufficient to allow introduction of the rabies virus. This can be particularly problematic regarding bites from bats, since their small, needle-like teeth can leave a wound so small as to go unnoticed (for example, if the person is a very sound sleeper) or to be disregarded by the person as "insignificant" (this problem is compounded by evidence that some bat-related rabies viruses might be able to establish infection after inoculation into superficial epidermal layers of the skin). Nonbite exposures include the introduction of saliva or other infectious material into a fresh, open wound or across a mucous membrane. **The combination of human rabies vaccine and human rabies immunoglobulin (HRIG) is recommended for both bite and nonbite exposures, with the exception of persons "previously vaccinated" (see below) who do not receive HRIG.** Intact skin is an effective barrier to the rabies virus, and the virus would not be expected to cross through a scabbed-over wound. The only infectious materials in a rabid animal are saliva and nervous tissues. Blood, urine, and feces from a rabid animal are not infectious.

   b) Species of Biting Animal:

      1) Skunks are the terrestrial carnivores most often infected with rabies in Missouri. Foxes, coyotes, and raccoons are also relatively susceptible to rabies, but are not a reservoir species as are skunks. Suggestive clinical signs of rabies among wildlife cannot be interpreted reliably. All bites by such wildlife should be considered possible exposures to rabies virus. RPEP should be initiated as soon as possible following exposure to such wildlife, unless the animal is available for diagnosis and public health authorities are facilitating expeditious laboratory testing, or if the brain tissue from the animal has already tested negative. Wild terrestrial carnivores that are available for diagnostic testing should be euthanized as soon as possible (without unnecessary damage to the head), and the brain should be submitted for rabies testing. If the results are negative, RPEP is not necessary. Other factors that might influence the urgency of decision-making regarding the initiation of RPEP before diagnostic results are known include the general appearance and behavior of the animal, whether the encounter was provoked by the presence of a human, and the severity and location of bites.

      2) Bat-related strains are the most common rabies virus variants responsible for human rabies in the United States; therefore, any potential exposure to a bat requires a thorough evaluation. If the

evaluation finds the person experienced a "known exposure or significant potential exposure" (see below, "Testing of Animals for Rabies"), any bats involved should be safely collected, humanely euthanized, and submitted to the Missouri State Public Health Laboratory (MSPHL) for rabies testing. Less than 1% of bats in the wild are rabid and only about 3% of the bats submitted to MSPHL for testing are found to be rabid. Timely diagnostic assessments rule out the need for unnecessary prophylaxis. The risk of rabies resulting from an encounter with a bat might be difficult to determine because of the limited injury inflicted by a bat bite (compared with more obvious wounds caused by the bite of terrestrial carnivores), an inaccurate recollection of a bat encounter that might have occurred several weeks or months earlier, and evidence that even a minor wound is sufficient for the transmission of some bat strains of rabies virus. For these reasons, any direct contact between a human and a bat should be evaluated for an exposure. If the person can be reasonably certain a bite, scratch, or mucous membrane exposure did not occur, or if the bat was tested and found to be negative for the presence of rabies virus, RPEP is not necessary.

Other situations that might qualify as exposures include finding a bat in the same room as a person who might be unaware that a bite or direct contact had occurred (e.g., a deeply sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person). These situations should not be considered exposures if rabies is ruled out by diagnostic testing of the bat, or circumstances suggest it is unlikely that an exposure took place. Other household members who did not have direct contact with the bat or were awake and aware when in the same room as the bat should not be considered as having been exposed to rabies. Circumstances that make it less likely that an undetected exposure occurred include the observation of bats roosting or flying in a room open to the outdoors, the observation of bats outdoors or in a setting where bats might normally be present, or situations in which the use of protective covers (e.g., mosquito netting) would reasonably be expected to preclude unnoticed contact. Clustering of human cases associated with bat exposures has never been reported in the United States (e.g., within the same household or among a group of campers where bats were observed during their activities). **In the event that RPEP is indicated in the absence of a visible wound (e.g., presumed bat bite), the combination of human rabies vaccine and HRIG is recommended, with the exception of persons "previously vaccinated" (see below) who do not receive HRIG. When HRIG is given under these circumstances, it should be injected intramuscularly (IM) in divided doses at sites distant from vaccine administration.**

3) Rodents and lagomorphs (rabbits and hares), either wild or domestic, present a very low risk for rabies exposure to humans. While the Centers for Disease Control and Prevention (CDC) reports a very small number of rabid wild rodents/lagomorphs each year, there have been no documented cases of transmission of rabies from any of these species to humans in the United States. Each rodent/lagomorph bite to a person should be evaluated individually, but RPEP is rarely indicated (even when the biting animal is not available for testing). A possible exception is when the biting rodent is a large species, such as a groundhog or beaver. These species might be large enough to survive the attack by another rabid animal and eventually develop rabies and pose a risk. Neither of these species has been found rabid in Missouri. Medical providers should consult with local or state public health officials as needed regarding bites from rodents and lagomorphs.

4) Dogs, cats, ferrets, and equids (horses, donkeys, mules, zebras) that have bitten a person may be quarantined for a ten-day period. The animal must be free of signs of rabies and the incident must have been provoked for the animal to be quarantined. An unprovoked attack by an animal might be more likely than a provoked attack to indicate that the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as provoked. The animal does not have to have a current rabies vaccination to be quarantined. Animals without a current rabies vaccination that inflict a provoked bite should be quarantined

under the supervision of the local health or animal control authority at a veterinary facility or animal impoundment facility. Situations in which an animal without a current rabies vaccination inflicts an unprovoked bite should be assessed by health authorities after the animal has been evaluated by a veterinarian to determine if rabies testing is needed in lieu of quarantine. Animals with current rabies vaccinations should still be quarantined for a ten-day period since no vaccine is 100% effective, but these quarantines can typically be conducted at the animal owner's home under the supervision of the local health or animal control authority. The ten-day quarantine period begins with the date of the bite. If the animal is healthy at the end of this period, the patient does not need RPEP and the animal can be released from quarantine. If signs suggestive of rabies develop during the quarantine period, RPEP of the bite victim should be initiated. The animal should be tested for rabies and, if results are negative, RPEP can be discontinued. If the animal is a stray or no longer wanted by the owner, it can be euthanized and tested for rabies in lieu of the ten-day quarantine. Quarantine of other domestic animals (e.g., cattle) is determined on a case-by-case basis through consultation with local or state public health officials. Quarantine periods are not recognized for wild animals or wild-domestic animal crosses (for example, wolf-dog hybrids); they are, instead, euthanized and tested for rabies. Quarantine or euthanasia/testing should be used to rule out the need for RPEP whenever possible to avoid needless treatment of animal bite victims.

c) Severity and Location of the Wound: The deeper the wound and closer to the central nervous system (or highly innervated tissue), the shorter the incubation period (and hence, the more quickly a decision must be made whether to initiate RPEP). There is no specified time period within which RPEP must be initiated to be effective; however, RPEP should begin as soon as possible after a thorough risk assessment has been conducted and the need for RPEP established. The average incubation period for rabies in humans is one to three months, but can range out to many months or even years (CDC has recorded two human cases with seven-year incubation periods). **If indicated, RPEP should be administered regardless of the length of any delay, provided the patient is not symptomatic. This includes the administration of both human rabies vaccine and HRIG, with the exception of persons "previously vaccinated" (see below) who do not receive HRIG.**

d) Circumstances Surrounding the Incident (Provoked or Unprovoked): This should be assessed from the "perspective" of the animal and not the patient (e.g., a person's movements in reaching out to pet a dog could be perceived as an aggressive action by the animal, resulting in a defensive bite). An "unprovoked" bite could be a symptom of rabies or it could result from another cause, such as other disease, the animal's individual disposition, or aggressive training by the owner. Many human/animal encounters are "provoked" by the person, such as approaching stray dogs/cats and feeding or handling wild animals.

Testing of Animals for Rabies

In Missouri, animal rabies testing is conducted only at MSPHL in Jefferson City. Specimens are normally prepared for submission by veterinarians, animal control agencies, or several of the larger local health departments that have veterinarians on staff. These entities are equipped to properly prepare the animal sample and have approved shipping containers designed for rabies specimen submission. Laboratory policy requires that only the animal head be submitted, except for bats and small rodents. MSPHL provides a free courier service that picks up boxed specimens each weekday from local health departments and select other facilities. Test results are normally available within one working day after delivery to the laboratory. There is no charge for testing, specimen boxes, or courier service. A charge could be incurred if a veterinarian is involved with specimen preparation. Payment of such charges varies by situation (for example, the owner – if there is one – normally pays for veterinary services). **Rabies testing should be requested only in those situations where a public health or medical decision needs to be made. Specimens should not be submitted purely for surveillance purposes or at the insistence of persons with a perceived but**

unfounded rabies risk. The DHSS policy letter with criteria for specimen submission may be found at www.health.mo.gov/lab/pdf/rabies_testing_policy.pdf**. Instructions for submitting specimens and complete animal rabies testing information (including a list of courier pick-up sites) may be found at** www.health.mo.gov/lab/rabies.php**.**

Treatment of Wounds

Immediate gentle irrigation with water or a dilute water povidone-iodine solution markedly decreases the risk for viral and bacterial infection following bite wounds. Wound cleansing is especially important in rabies prevention because thorough wound cleansing alone without other RPEP markedly reduces the likelihood of rabies in animal studies. Consideration should be given to the need for a booster dose of tetanus vaccine. Decisions regarding the use of antibiotic prophylaxis and primary wound closure should be individualized on the basis of the exposing animal species, size and location of the wound(s), and time interval since the bite. Suturing should be avoided, when possible.

RPEP: General Considerations

1. RPEP is indicated for persons with a known exposure or significant potential exposure to a rabid animal. Except in extremely high-risk situations, RPEP does not need to be immediately administered if the biting animal is available for rabies testing or quarantine. A negative rabies test means the patient does not require RPEP. Quarantines apply only to dogs, cats, ferrets, and equids (horses, mules, donkeys, zebras). Other domestic animals may be quarantined on a case-by-case basis after consultation with local or state public health officials. Wild animals and wild/domestic animal crosses are not quarantined; instead, they are euthanized and tested.

2. Administration of RPEP is typically a medical urgency, not a medical emergency. Although RPEP has not always been properly administered in the United States, no failures have been documented since current biologics have been licensed. RPEP should always include both vaccine and HRIG, with the exception of persons who have been "previously vaccinated" (see below); these persons do not receive HRIG.

3. For previously vaccinated persons (see below) who are exposed to rabies, determining the rabies virus neutralizing antibody titer for decision-making about prophylaxis is NOT appropriate.

4. Two rabies vaccines are available for use in the United States; either can be administered with HRIG at the beginning of RPEP. Testing of patients completing RPEP is not necessary to document seroconversion unless the person is immunosuppressed.

5. Rabies vaccines are approved and licensed for use in dogs, cats, ferrets, horses, cattle, and sheep. Rabies is rare in properly vaccinated animals. By Missouri statute, rabies vaccine must be administered by a licensed veterinarian. Rabies vaccines are available to the general public and some persons choose to vaccinate their own pets. However, due to the many variables involved in achieving and maintaining a protective vaccination response in animals, the rabies vaccination history of an animal is considered dependable for making RPEP decisions only when vaccine has been administered by a licensed veterinarian. There are no vaccines licensed for use in other domestic animals or for any wild animals or wild/domestic animal crosses.

Rabies Post-Exposure Prophylaxis Schedule

Reference: *Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies, Recommendations of the Advisory Committee on Immunization Practices* (www.cdc.gov/mmwr/pdf/rr/rr5902.pdf).

Not previously vaccinated	Wound cleansing	All RPEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidone-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (IM) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because HRIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered. HRIG should be administered on day 0[§]. If HRIG was not given when vaccination was begun, it can be given up to and including day 7 of the RPEP series.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area[†]), 1 each on days 0[§], 3, 7, and 14[¶].
Previously vaccinated**	Wound cleansing	All RPEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidone-iodine solution) should be used to irrigate the wounds.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area[†]), 1 each on days 0[§] and 3.

* These regimens are applicable for persons in all age groups, including children.

† The deltoid area is the only acceptable site for vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area (this contraindication does not apply to administration of HRIG).

§ Day 0 is the day dose 1 of vaccine is administered.

¶ For persons with immunosuppression, RPEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

**Any person who has ever received one of the complete pre-exposure or post-exposure regimens of HDCV, PCECV, or rabies vaccine adsorbed (RVA; RVA is no longer available in the U.S.), or previous vaccination with any other type of rabies vaccine and documented history of antibody response to the prior vaccination.

RPEP Consultation With Local or State Health Departments

Assistance with animal bite/potential rabies exposures may be obtained from local public health agencies (see www.health.mo.gov/living/lpha/lphas.php for a list of local public health agencies and contact information) or from the Missouri Department of Health and Senior Services (DHSS) (Monday through Friday, 8:00 AM to 5:00 PM, telephone 573/526-4780; after hours and weekends telephone 800/392-0272). When consulting with local or state public health officials, medical providers should have the following information available:

1. Type of exposure (examples: bite, mucous membrane, “bat in the house,” etc.).
2. Circumstances surrounding the incident (example: child petting stray cat).
3. Date of incident.

4. Nature of wound (puncture versus scratch, location on body, severity, etc.).
5. Species of animal involved.
6. Patient name, address, telephone number.
7. Animal owner (if applicable) name, address, telephone number.
8. Location of animal following incident.
9. Apparent health and behavior of animal.
10. Rabies vaccination status of animal, if applicable (rabies vaccines are licensed only for dogs, cats, ferrets, horses, cattle, and sheep).
11. Has patient been "previously vaccinated" against rabies? (See "Rabies Post-Exposure Prophylaxis Schedule" above.)

Deviations From Recommended RPEP Vaccination Schedule

Every attempt should be made to adhere to the recommended vaccination schedule. Once vaccination is initiated, delays of a few days for individual doses are unimportant, but the effect of longer lapses of weeks or more is unknown. Most interruptions in the vaccine schedule do not require reinitiation of the entire series. For most minor deviations from the schedule, vaccination can be resumed as though the patient were on schedule. For example, if a patient misses the dose scheduled for Day 3 and presents for vaccination on Day 5, the Day 3 dose should be administered that day and the schedule resumed, maintaining the same interval between doses. In this scenario, the remaining doses would be administered on days 9 and 16. When substantial deviations from the schedule occur, immune status should be assessed by performing serologic testing 7–14 days after administration of the final dose in the series.

RPEP Precautions

Immunosuppressive agents, antimalarials, and immunosuppressive diseases can interfere with active immunity following vaccination. Immunosuppressive agents should not be administered during RPEP unless essential for the treatment of other conditions. When RPEP is administered to an immunosuppressed person, one or more serum samples should be tested for rabies virus neutralizing antibody to ensure that an acceptable antibody response has developed. If no acceptable antibody response is detected, the patient should be managed in consultation with appropriate public health officials.

RPEP Contraindications

Persons who have a history of serious hypersensitivity to components of rabies vaccine or to other vaccines with components that are also present in rabies vaccine should be revaccinated with caution. Dietary intolerance to eggs is not a contraindication to immunization with human rabies vaccine. Because of the potential consequences of inadequately managed rabies exposure, pregnancy is not considered a contraindication to RPEP. Studies have indicated no increased incidence of abortion, premature births, or fetal abnormalities associated with rabies vaccination. Rabies exposure or the diagnosis of rabies in the mother should not be regarded as reasons to terminate the pregnancy.

Sources of Human Rabies Vaccine and HRIG

Human rabies vaccine and HRIG are not available through DHSS and are typically not available through local public health agencies. Medical providers may contact their local public health agency to determine if vaccine and HRIG are available through the latter. Contact information for local public health agencies can be found at www.health.mo.gov/living/lpha/lphas.php. Medical providers and pharmacies can order human rabies vaccine and HRIG directly from manufacturers and distributers. Product and contact information is provided in the following table:

Currently Available Rabies Biologics – United States		
Human Rabies Vaccine	**Product Name**	**Manufacturer**
Human diploid cell vaccine (HDCV)	Imovax® Rabies	Sanofi Pasteur Telephone: 800/822-2463 www.sanofipasteur.us/vaccines
Purified chick embryo cell vaccine (PCECV)	RabAvert®	Novartis Vaccines Telephone: 800/244-7668 www.novartisvaccinesdirect.com
Rabies Immunoglobulin	**Product Name**	**Manufacturer**
	Imogam® Rabies-HT	Sanofi Pasteur Telephone: 800/822-2463 www.sanofipasteur.us/vaccines
	HyperRab™ S/D	Grifols USA Telephone: 800/243-4153 www.grifols.com/en/web/eeuu/bioscience/-/product/hyperrabb_s_d_rabies_immune-globulin

For information regarding human rabies vaccine and HRIG availability, refer to www.cdc.gov/rabies/resources/availability.html. Patient assistance programs that provide vaccine and HRIG for uninsured/underinsured patients are available; refer to www.cdc.gov/rabies/medical_care/programs.html.

Suspected Case of Human Rabies

1. Patient history, signs/symptoms, duration and progression of illness, and laboratory test results for other common etiologies of encephalitis will help determine if rabies should be on the differential diagnosis list for a patient, and thus whether ante-mortem rabies testing should be considered (see below). Patient history is important to identify a possible exposure to rabies and other encephalitides; however, rabies should never be ruled out based solely on the absence of a definite exposure history.

2. Rabies should be considered in patients with signs or symptoms of encephalitis or myelitis, including autonomic instability, dysphagia, hydrophobia, paresis, and paresthesia, particularly if a nonspecific prodrome preceded the onset of these signs by three to four days. Progressive worsening of neurologic signs is characteristic of rabies and should be considered as a positive indicator for rabies.

3. Laboratory tests to rule out common encephalitides (herpes, enteroviruses, arboviruses) should be performed. Negative results of these tests would increase the likelihood of rabies as the diagnosis. If a patient presents with symptoms similar to the ones described above, but the neurologic status does not change and the illness continues for longer than three weeks, rabies is unlikely as the diagnosis.

4. Positive Indicators for Rabies:

   a) Nonspecific prodrome prior to onset of neurologic signs.
   b) Neurologic signs consistent with encephalitis or myelitis (dysphagia, hydrophobia, paresis).
   c) Progression of neurologic signs.
   d) Negative test results for other etiologies of encephalitis.

5. Negative Indicators for Rabies:

   a) Improvement or no change in neurologic status.
   b) Illness with $\geq$ 2 to 3 week duration.

6. Laboratory Testing of Human Specimens for Rabies: Ante-mortem testing of human specimens is conducted by CDC, but submission of specimens must be coordinated through MSPHL. The Rabies Section at MSPHL may be contacted by calling 573/751-3334; after hours and weekends, call 800/392-0272 (refer also to www.health.mo.gov/lab/rabies.php). The following four samples are required by CDC to provide an ante-mortem rule out of rabies: saliva, neck biopsy, serum, cerebrospinal fluid. A rule out cannot be provided if all samples are not collected. Information regarding specimen collection/submission can be found at the following CDC website: www.cdc.gov/rabies/specific_groups/doctors/ante_mortem.html.

7. Management of Human Rabies: Clinicians faced with treating clinical rabies patients can either offer supportive therapy or an aggressive treatment plan. There is no single effective treatment for rabies once clinical signs are evident. Resources shown on the CDC website - www.cdc.gov/rabies/specific_groups/doctors/human_rabies.html - provide current research findings and thoughts regarding treatment options. They are not intended to serve as recommendations for rabies treatment. Consultation with medical staff at DHSS can be accessed by calling 573/526-4780; after hours and weekends, call 800/392-0272.

Reportable Conditions

In accordance with 19 CSR 20-20.020, *Reporting Communicable, Environmental and Occupational Diseases* (www.sos.mo.gov/adrules/csr/current/19csr/19c20-20.pdf), the following conditions are reportable to the local public health agency or DHSS by telephone, facsimile, or other rapid communication. Contact information for local public health agencies can be found at www.health.mo.gov/living/lpha/lphas.php. DHSS can be contacted Monday through Friday, 8:00 AM to 5:00 PM, telephone 573/751-6113; after hours and weekends, call 800/392-0272 or fax 573/526-0235.

1. *Rabies (Human)*: Immediately upon first knowledge or suspicion.
2. *Animal (mammal) bite, wound, humans*: Within one day of first knowledge or suspicion.
3. *Rabies (Animal)*: Within one day of first knowledge or suspicion.
4. *Rabies Post-Exposure Prophylaxis (Initiated):* Within three days of first knowledge or suspicion.

"An Ounce of Prevention….."

To help prevent rabies exposures in your community, please refer your health education staff to the following DHSS website where they can order free educational posters: /www.health.mo.gov/living/healthcondiseases/communicable/tickscarrydisease/orderform.php

Websites

1. Missouri Department of Health and Senior Services, *Rabies Surveillance*, www.health.mo.gov/living/healthcondiseases/communicable/rabies/index.php
2. CDC, *Rabies*, www.cdc.gov/rabies
3. CDC, *Rabies- Information for Doctors*, www.cdc.gov/rabies/specific_groups/doctors/index.html
4. CDC, *Rabies- Ante Mortem Testing*, www.cdc.gov/rabies/specific_groups/doctors/ante_mortem.html
5. CDC, *Rabies-Management of Human Rabies*, www.cdc.gov/rabies/specific_groups/doctors/human_rabies.html
6. *Human Rabies---Missouri, 2008, CDC Morbidity and Mortality Weekly Report (MMWR)*, November 6, 2009/58(43);1207-1209, www.cdc.gov/mmwr/preview/mmwrhtml/mm5843a3.htm

Questions regarding this Health Advisory should be directed to the DHSS Office of Veterinary Public Health at 573/526-4780 or 800/392-0272 (24/7).